REMARKS

Claims 1-22 and 24-34 were considered in the Office Action. Claims 21-22, 24, 27, and 31 were canceled. Claims 1, 2, 4, 9-12, 14, 25, 26, 30, and 32 have been amended. Accordingly, claims 1-20, 25, 26, 28-30, and 32-34 are presented for further examination.

Summary of Examiner Interview

On September 22, 2010, the undersigned and Examiner Negin conducted an Examiner interview to discuss proposed amendments to overcome the prior art rejections. Applicant proposed claims that are directed to a method for determining the extent of degradation of an RNA sample by, among other steps, extracting features from an electropherogram of the RNA sample. Applicant also discussed how the proposed claims differ from the Carbeck et al. and Negin et al. references. In particular, it was discussed how Carbeck et al. and Negin et al. do not disclose a method for determining the extent of degradation of an RNA sample. Examiner Negin conceded that such amendments would overcome the rejections based on Carbeck et al. and Negin et al. but stated that another search may be necessary to determine whether there is other prior art that anticipates or renders obvious the amended claims.

Objection to Declaration

The Examiner has objected to the declaration because "all of the copies of the declaration do not list each inventor." Applicant respectfully requests that the requirement for a new declaration be held in abeyance until such time that there is allowable subject matter. Because at least some of the inventors are no longer employed by the assignee of this application, applicant is anticipating that it may be time-consuming to have a new declaration executed.

Claim Rejections

All the previously pending claims were rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of (1) Carbeck et al. [Journal of the American Chemical Society, 1999, volume 121, pages 10671-79] in view of (2) Negin et al. [Journal of the American

Chemical Society, 2002, volume 124, pages 2911-16] as evidenced by the definition of "denatuation" from (3) Dorland's Illustrated Medical Dictionary, 2007, alone or in combination with additional references.

In order to advance prosecution and without conceding the propriety of the Examiner's rejections, applicants have amended the claims so that the claimed method is directed to determining the extent of degradation, expressed in terms of a quality value, of an RNA sample by separating the RNA sample by mobility, using an electrophoresis device, to generate an electropherogram, extracting features from the electropherogram, and determining the quality value from the extracted features using a quality algorithm. Applicants expressly reserve the right to pursue broader claims encompassing other biomolecules in a continuation application.

As the pending claims now all recite a method/apparatus/data carrier involving determining the extent of ***degradation*** of an ***RNA*** sample, the most pertinent rejections for the now pending claims from the Office Action are Rejections #8 and #9 which are directed to claims reciting the analysis of RNA samples. These rejections rely on a combination of (1) Carbeck et al. in view of (2) Negin et al. as evidence by the definition of "denaturation" from (3) Dorland's Illustrated Medical Dictionary, 2007 in view of (4) Goldsborough [WO 00/66605] in view of (5) Pan et al. [Journal of Molecular Biology, 1997, volume 273, pages 7-13], and for Rejection #9, in further view of (6) Strumberg et al. [Molecular and Cellular Biology, 2000, volume 20, pages 3977-3987]. Applicants submit that none of these references, alone or in combination, disclose a method of determining the degradation of any biomolecule, yet alone using an electropherogram to determine the extent of degradation of an RNA sample.

First, contrary to the Examiner's assertions, the combination of Carbeck et al., Negin et al., and Dorland does not disclose a claimed method of determining the extent of ***degradation*** of a biomolecule. Thus, the combination of these references with the RNA references – Goldsborough, Pan et al. and Strumberg et al. do not disclose the currently pending claims directed to a method of determining the extent of ***degradation*** of an RNA molecule.

The pending claims specifically recite a "method is for determining the extent of degradation." Accordingly, it is not clear to applicants why the Examiner is equating denaturation with degradation. As defined in the dictionary definition cited by the Examiner, protein denaturation is defined as "disruption of the configuration (tertiary structure) of a protein, as by heat, change in pH, or other physical or chemical means, resulting in alteration of the physical properties and loss of biological activity of the protein." However, degradation as used in the claims refers to the "breakage" of the RNA molecules in the sample by splitting off one or more group of atoms such that the length of the RNA molecules are shortened. "Denaturation" which involves changes in the ***configuration*** of a molecule is not the same as "degradation" which involves changes in the length of the biomolecule. Notably, in the same dictionary cited by the Examiner, "degradation" is defined as "conversion of a chemical compound to one less complex, ***as by splitting off one or more groups of atoms***. See also lysis." Dorland's Illustrated Medical Dictionary, 2007 (emphasis added). This definition of degradation as involving the splitting off of groups of atoms is consistent with how degradation is used in applicants' specification. For example, at page 1, lines 19-20, the specification equates degradation with the shortening of RNA polymers.

> [A] shift in the lengths of RNA polymers to shorter lengths is observed whenever degradation has occurred.

Similarly, at page 1, lines 29-34, applicants explained that the "quality" of an RNA sample can be understood as a measure of its "integrity" which in turn means that the RNA molecules have not suffered "degradation or breakage" and "have remained intact." Accordingly, "degradation" as used in the claims does not have the same meaning as "denaturation."

Neither Carbeck et al. nor Negin et al. disclose a method for determining the extent of ***degradation*** of a biomolecule. Carbeck et al. involves using a charge ladder of a protein sample to calculate other properties of the protein such as the charge of the native protein in solution or the mobility of the native protein. As the Examiner concedes, Carbeck et al. does not involved determining the extent of degradation of a biomolecule. Negin et al. again involves using a

charge ladder of a protein sample (run at two different temperatures) to determine the free energy of unfolding of the protein. Thus, Negin et al., at most, is directed to determining the extent of changes in the tertiary structure of the protein (i.e., denaturation) not the degradation of the protein (i.e., the shortening of the length of the protein). Because the combination of Carbeck et al. and Negin et al. does not disclose a method for determining the extent of degradation, for this reason alone, the rejections must be withdrawn.

Moreover, the primary references Carbeck et al. and Negin et al., among other features of the pending claims, do not disclose "collecting a statistically significant number of trial electropherograms covering a prescribed set of" biomolecule samples or "assigning a quality label . . . to every trial electropherogram." In the Action, the Examiner relies on Figure 1 of Carbeck et al. as disclosing this claimed step. See Office Action at page 6. However, Figure 1 shows a ***single*** electropherogram for a single protein sample. For example, claims 1, 25, 26, and 28 as amended require a statistically significant number of trial electropherograms. Moreover, the quality label is assigned to each trial electropherogram, not to "each point of measured data" as stated by the Examiner. See Office Action at page 6. In an embodiment of claimed method, the number of trial electropherograms "should be as large as possible." See specification at page 5, lines 8-10.

For example, Figures 3a-3f of the present application show electropherograms of various qualities which would be expected in the statistically significant number of trial electropherograms collected. Each of these electropherograms would be assigned a quality label as explained in the specification at page 5, lines 16-22. Carbeck et al. and Negin et al. are directed to completely different methods.

Second, the RNA references – Goldsborough, Pan et al. and Strumberg et al. – do not remedy the deficiencies of Carbeck et al. and Negin et al. As noted by the Examiner, Goldsborough is directed to certain modifications that can be made to RNA molecules. Pan et al. is directed to understanding the folding of RNA. Neither Goldsborough nor Pan et al. are directed to a method of determining the extent of degradation of an RNA sample, and thus these

references do not remedy the deficiencies of Carbeck et al. and Negin et al. discussed above. The Examiner cites to Strumberg et al. (in particular Figure 1) as disclosing the "eight segments" of RNA of claim 10 and "the ratios of the areas of the 18S to the 28S fragment" of claim 14. See Office Action at page 24. Strumberg et al. does not disclose the "segments" and the "ratios" as those terms are used in applicants' pending claims. The eight segments of claim 10 refer to segments of the *measured data* (now amended to recite "electropherogram") not the segments of the RNA ***gene***. This is best understood by reference to Figure 1 of the present application and the description on page 14, lines 1-3. Likewise, the ratios recited in claim 14 again refer to the ratios of the areas of certain segments of the trial measured data (or electropherogram). The segments show in Figure 1 of Strumberg et al. are segments of an rRNA gene. Accordingly, Strumberg et al. is not relevant to the presently claimed invention and thus cannot cure the deficiencies discussed above.

Accordingly, applicants respectfully request that all the obviousness rejections be withdrawn.

Conclusion

In view of the foregoing remarks, applicant respectfully requests that the Examiner withdraw the pending objections and rejections and issue a Notice of Allowance.

If any issues remain, applicant requests that the Examiner contact the undersigned to discuss.

Respectfully submitted,

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